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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/089,501

04/22/2002

Hiroyuki Saito

053466-0325

9449

22428 7590 11/10/2010
FOLEY AND LARDNER LLP
SUITE 500
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WASHINGTON, DC 20007

EXAMINER

HAMUD, FOZIA M

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

11/10/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/089,501	Applicant(s) SAITO ET AL.	
	Examiner FOZIA M. HAMUD	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 60-62 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 60-62 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 March 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1a. Receipt of Applicants' amendment and arguments, filed on 03 August 2010 is acknowledged.

Status of Claims:

1b. Claims 60-62 are pending and under consideration.

Response to Applicants' amendment and arguments:

Specification:

2a. The new abstract, which is limited to a single paragraph is acknowledged.

2b. The rejection of claims 45-49, 52, 53 and 55 made under 35 U.S.C. 102(e) as being anticipated by Wong et al (U.S. Patent 5,986,065, EFD 3/10/1997), is withdrawn. The Wong et al reference does not teach the use of an antibody comprising the heavy and light variable chains recited in instant claims 60-62.

2c. The indicated allowability of claims 51, 54 and 56 is withdrawn, in light of the following rejection.

Priority:

3a. This application, filed 4/22/2002 claims priority to PCT/JP00/06802, filed 9/29/2000, therefore the instant invention has been granted a priority date of 9/29/2000.

Foreign Priority:

3b. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. However, it is noted that Applicants cannot rely upon the foreign priority papers, because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Art Unit: 1647

Claim Rejections - 35 USC § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 60-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claims recite "...an antibody that binds to an inhibitory site for binding a complex of human tissue factor and factor VIIa to factor X, upon binding human TF", which renders the claims indefinite, because it is unclear whether the administered antibody binds to tissue factor and thus inhibits the formation of a tissue factor-Factor VII and Factor X complex, **or** whether it binds to an ***inhibitory site*** for binding a complex of tissue factor-Factor VII and Factor X and if so, which inhibitory site? Appropriate correction is required.

Claim Rejections - 35 USC § 102:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 60-62 are rejected under 35 U.S.C. 102(e) as being anticipated by Sato et al (U.S. Patent 6,677,436, EFD 04/22/1999; cited in the notice of reference cited by Examiner submitted on 02/04/2010).

Claims 60-62 are drawn to a method for suppressing hypertrophy of the vascular intima caused by expression of tissue factor in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of an antibody that binds to an inhibitory site for binding a complex of human tissue factor (human TF) and Factor VIIa to Factor X, upon binding to human TF, wherein the antibody comprises the heavy and light chain pair set forth in amino acid sequence set forth in SEQ ID NO:29 and SEQ ID NO:88, (b-b); SEQ ID NO:59 and SEQ ID NO:98, (i-b), or SEQ ID NO:59 and SEQ ID NO:88, (i-b2).

It is also noted that as discussed at page 7 of the previous Office Action of 04 February 2010, the instant specification does not define "hypertrophy of the vascular intima". Based upon the definitions of "hypertrophy" and "vascular intima" known in the art (see Stedman's Medical Dictionary 27th Edition), the Examiner has interpreted this phrase as meaning that the expression of tissue factor causes irregular formations or thickening of blood vessels.

SATO, et al reference (U.S. Patent No. 6,677,436), teaches a humanized antibody or a chimeric antibody, (designated as b-b, i-b or i-b2), which comprises the same heavy and light chain sequences as recited in claims 60-62, (see SEQ ID NO:166, SEQ ID NO:173, SEQ ID NO:180, and SEQ ID NO:173, which are identical to SEQ ID NOs: 29, 88, 59 and 98, respectively). Also see the attached SEQUENCE COMPARISON "A-D". The antibodies taught by Sato et al bind human TF and ***inhibit the activation*** of Factor X by the TF/Factor VIIa complex, and can be used for the treatment of disseminated intravascular coagulation, (DIC), (See the abstract, Figure

Art Unit: 1647

32, column 27, lines 49-56, column 52, line 60 to column 63, line 4, columns 54-55).

DIC is a disease in which the activation of the coagulation system in a blood vessel leads to systemic multiple occurrence of blood clots, mainly in the microvasculature (column 1, lines 47-50). It is recognized in the relevant art that TF is involved in the etiology of DIC. For example, Asakura et al, (Thrombosis Research, 1995, Vol. 80, No. 3, pages 217-224), teach that significant elevation of plasma antigen levels of TF was observed in cases of DIC and that levels of TF were decreased with the clinical improvement in some cases of DIC, but were further increased or remained at high levels in patients who showed no improvement of DIC, (see abstract and page 223). See also Sako et al. column 2, lines 1-3.

A compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169 USPQ 226 (CCPA 1971)).

Therefore, the Sato et al reference anticipates instant claims 60-62 in the absence of any evidence on the contrary.

SEQUENCE COMPARISON "A"

Title: US-10-089-501-29
Perfect score: 734
Sequence: 1 MKCSWVIFFLMAVVTGVNSQ.....SGYAMDYWGQGTTLVTVSSAS 138

US-09-647-468-166
; Sequence 166, Application US/09647468
; **Patent No. 6677436**
; GENERAL INFORMATION:
; APPLICANT: SATO, KOH
; APPLICANT: ADACHI, HIDEKI
; APPLICANT: YABUTA, NAOHIRO

Art Unit: 1647

```
; TITLE OF INVENTION: HUMANIZED ANTIBODY AGAINST HUMAN TISSUE FACTOR (TF)
AND
; TITLE OF INVENTION: PROCESS OF PRODUCTION OF THE HUMANIZED ANTIBODY
; FILE REFERENCE: 053466/0289
; CURRENT APPLICATION NUMBER: US/09/647,468
; CURRENT FILING DATE: 2000-09-29
; PRIOR APPLICATION NUMBER: PCT/JP99/01768
; PRIOR FILING DATE: 1999-04-02
; PRIOR APPLICATION NUMBER: JP 10-91850
; PRIOR FILING DATE: 1998-04-03
; NUMBER OF SEQ ID NOS: 183
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 166
; LENGTH: 138
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Amino acid
; OTHER INFORMATION: sequence coding of version "b" of humanized H
; OTHER INFORMATION: chain V region
US-09-647-468-166
```

```
Query Match          100.0%; Score 734; DB 2; Length 138;
Best Local Similarity 100.0%; Pred. No. 4.8e-64;
Matches 138; Conservative 0; Mismatches 0; Indels 0; Gaps
0;
```

```
Qy          1 MKCSWVIFFLMAVVTGVNSQVQLLESGAVLARPGTSVKISCKASGFNIKDYMHVVKQRP 60
|
Db          1 MKCSWVIFFLMAVVTGVNSQVQLLESGAVLARPGTSVKISCKASGFNIKDYMHVVKQRP 60
```

```
Qy          61 GQGLEWIGGNDPANGHSMYDPKFQGRVTITADTSTNTAYMELSSLRSEDTAIYYCARD SG
120
|
Db          61 GQGLEWIGGNDPANGHSMYDPKFQGRVTITADTSTNTAYMELSSLRSEDTAIYYCARD SG
120
```

```
Qy          121 YAMDYWGQGLTVTVSSAS 138
|
Db          121 YAMDYWGQGLTVTVSSAS 138
```

SEQUENCE COMPARISON "B"

```
Title:          US-10-089-501-59
Perfect score:  731
Sequence:       1 MKCSWVIFFLMAVVTGVNSQ.....SGYAMDYWGQGLTVTVSSAS 138
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RESULT 1

US-09-647-468-173

```
; Sequence 173, Application US/09647468
; Patent No. 6677436
; GENERAL INFORMATION:
```

Art Unit: 1647

```

; APPLICANT: SATO, KOH
; APPLICANT: ADACHI, HIDEKI
; APPLICANT: YABUTA, NAOHIRO
; TITLE OF INVENTION: HUMANIZED ANTIBODY AGAINST HUMAN TISSUE FACTOR (TF)
AND
; TITLE OF INVENTION: PROCESS OF PRODUCTION OF THE HUMANIZED ANTIBODY
; FILE REFERENCE: 053466/0289
; CURRENT APPLICATION NUMBER: US/09/647,468
; CURRENT FILING DATE: 2000-09-29
; PRIOR APPLICATION NUMBER: PCT/JP99/01768
; PRIOR FILING DATE: 1999-04-02
; PRIOR APPLICATION NUMBER: JP 10-91850
; PRIOR FILING DATE: 1998-04-03
; NUMBER OF SEQ ID NOS: 183
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 173
; LENGTH: 138
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Amino acid
; OTHER INFORMATION: sequence coding of version "i" of humanized H
; OTHER INFORMATION: chain V region
US-09-647-468-173

```

```

Query Match          100.0%; Score 731; DB 2; Length 138;
Best Local Similarity 100.0%; Pred. No. 4.8e-60;
Matches 138; Conservative 0; Mismatches 0; Indels 0; Gaps
0;

```

```

Qy      1 MKCSWVIFFLMAVVTGVNSQVQLLESGLAVLARGTSVKISCKASGFNIKDYMHVVKQRP 60
          |||
Db      1 MKCSWVIFFLMAVVTGVNSQVQLLESGLAVLARGTSVKISCKASGFNIKDYMHVVKQRP 60

Qy      61 GQGLEWIGGNDPANGHSMYDPKFQGRVTITADTSTSTVFMELSSLRSED TAVYYCARD SG
120
          |||
Db      61 GQGLEWIGGNDPANGHSMYDPKFQGRVTITADTSTSTVFMELSSLRSED TAVYYCARD SG
120

Qy      121 YAMDYWGQGT LVT VSSAS 138
          |||
Db      121 YAMDYWGQGT LVT VSSAS 138

```

SEQUENCE COMPARISON "C"

```

Title:      US-10-089-501-88
Perfect score: 670
Sequence:    1 MRAPAQFFGILLWFP GIRC.....CLQHGESPYTFGGG TKVEIK 127

```

RESULT 1

Art Unit: 1647

US-09-647-468-180

```
; Sequence 180, Application US/09647468
; Patent No. 6677436
; GENERAL INFORMATION:
; APPLICANT: SATO, KOH
; APPLICANT: ADACHI, HIDEKI
; APPLICANT: YABUTA, NAOHIRO
; TITLE OF INVENTION: HUMANIZED ANTIBODY AGAINST HUMAN TISSUE FACTOR (TF)
AND
; TITLE OF INVENTION: PROCESS OF PRODUCTION OF THE HUMANIZED ANTIBODY
; FILE REFERENCE: 053466/0289
; CURRENT APPLICATION NUMBER: US/09/647,468
; CURRENT FILING DATE: 2000-09-29
; PRIOR APPLICATION NUMBER: PCT/JP99/01768
; PRIOR FILING DATE: 1999-04-02
; PRIOR APPLICATION NUMBER: JP 10-91850
; PRIOR FILING DATE: 1998-04-03
; NUMBER OF SEQ ID NOS: 183
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 180
; LENGTH: 127
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Nucleotide
; OTHER INFORMATION: sequence coding of version "b" of humainzed L
; OTHER INFORMATION: chain V region
US-09-647-468-180
```

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Query Match          100.0%; Score 670; DB 2; Length 127;
Best Local Similarity 100.0%; Pred. No. 1.2e-51;
Matches 127; Conservative 0; Mismatches 0; Indels 0; Gaps
0;
```

```
Qy      1 MRAPAQFFGILLWFPGIRCDIQMTQSPSSLSASVGDRVITITCKASQDIKSFLSWYQQKP 60
          |||
Db      1 MRAPAQFFGILLWFPGIRCDIQMTQSPSSLSASVGDRVITITCKASQDIKSFLSWYQQKP 60
```

```
Qy      61 GKAPKLLIYYATSLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCLQHGESPYTFGG
120
          |||
Db      61 GKAPKLLIYYATSLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCLQHGESPYTFGG
120
```

```
Qy      121 GTKVEIK 127
          |||
Db      121 GTKVEIK 127
```

SEQUENCE COMPARISON "D"

```
Title:           US-10-089-501-98
Perfect score:    669
Sequence:        1 MRAPAQFFGILLWFPGIRC.....CLQHGESPYTFGGGTKVEIK 127
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US-09-647-468-183

; Sequence 183, Application US/09647468
; **Patent No. 6677436**
; GENERAL INFORMATION:
; APPLICANT: SATO, KOH
; APPLICANT: ADACHI, HIDEKI
; APPLICANT: YABUTA, NAOHIRO
; TITLE OF INVENTION: HUMANIZED ANTIBODY AGAINST HUMAN TISSUE FACTOR (TF)
AND
; TITLE OF INVENTION: PROCESS OF PRODUCTION OF THE HUMANIZED ANTIBODY
; FILE REFERENCE: 053466/0289
; CURRENT APPLICATION NUMBER: US/09/647,468
; CURRENT FILING DATE: 2000-09-29
; PRIOR APPLICATION NUMBER: PCT/JP99/01768
; PRIOR FILING DATE: 1999-04-02
; PRIOR APPLICATION NUMBER: JP 10-91850
; PRIOR FILING DATE: 1998-04-03
; NUMBER OF SEQ ID NOS: 183
; SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 183
; LENGTH: 127
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence: Amino acid
; OTHER INFORMATION: sequence coding for version "b2" of humainzed L
; OTHER INFORMATION: chain V region
US-09-647-468-183

Query Match 100.0%; Score 669; DB 2; Length 127;
Best Local Similarity 100.0%; Pred. No. 3.8e-54;
Matches 127; Conservative 0; Mismatches 0; Indels 0; Gaps
0;

Qy	1	MRAPAQFFGILLWFPGIRCDIQMTQSPSSLSASVGDRVTITCKASQDIKSFLSWYQQKP	60
Db	1	MRAPAQFFGILLWFPGIRCDIQMTQSPSSLSASVGDRVTITCKASQDIKSFLSWYQQKP	60
Qy	61	EKAPKSLIYYATSLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCLQHGESPYTFGG	
120			
Db	61	EKAPKSLIYYATSLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCLQHGESPYTFGG	
120			
Qy	121	GTKVEIK	127
Db	121	GTKVEIK	127

Conclusion:

Art Unit: 1647

6. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FOZIA M. HAMUD whose telephone number is (571)272-0884. The examiner can normally be reached on Monday-Friday: 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
03 November 2010

/Bridget E Bunner/
Primary Examiner, Art Unit 1647